

Fig. 1

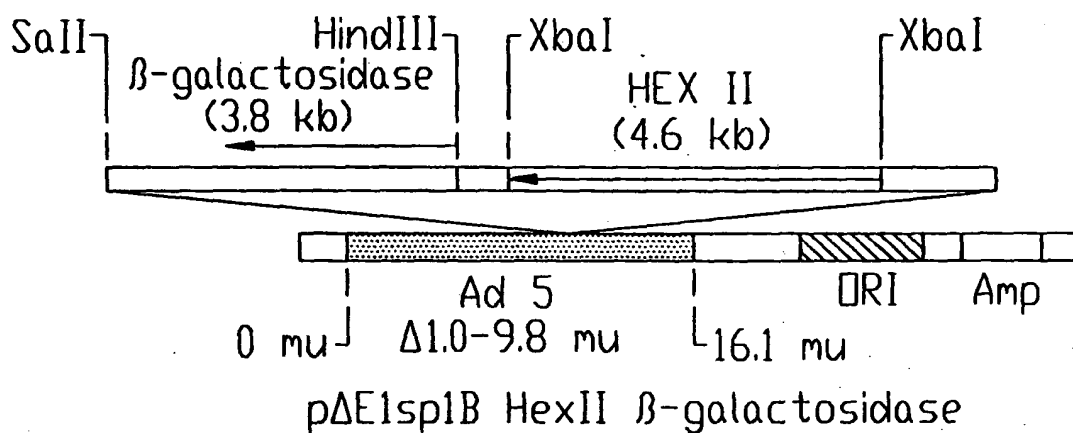


Fig. 2

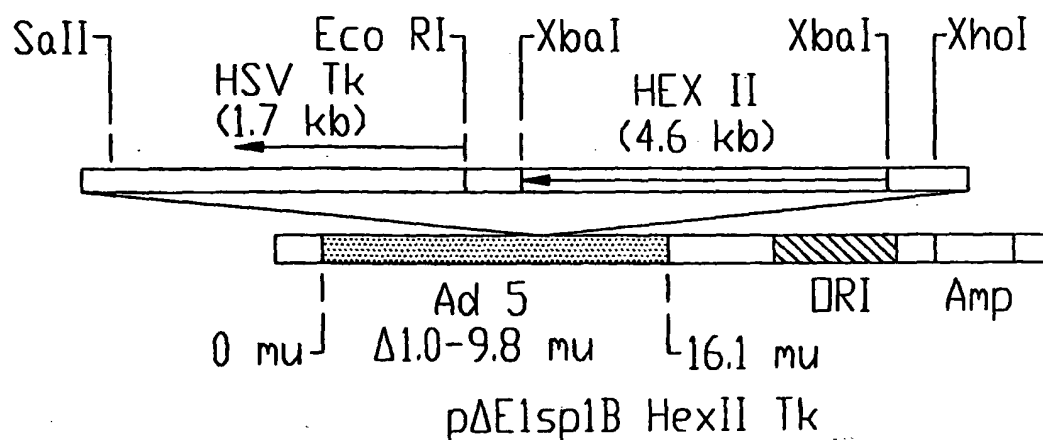


Fig. 3

009727 2262460

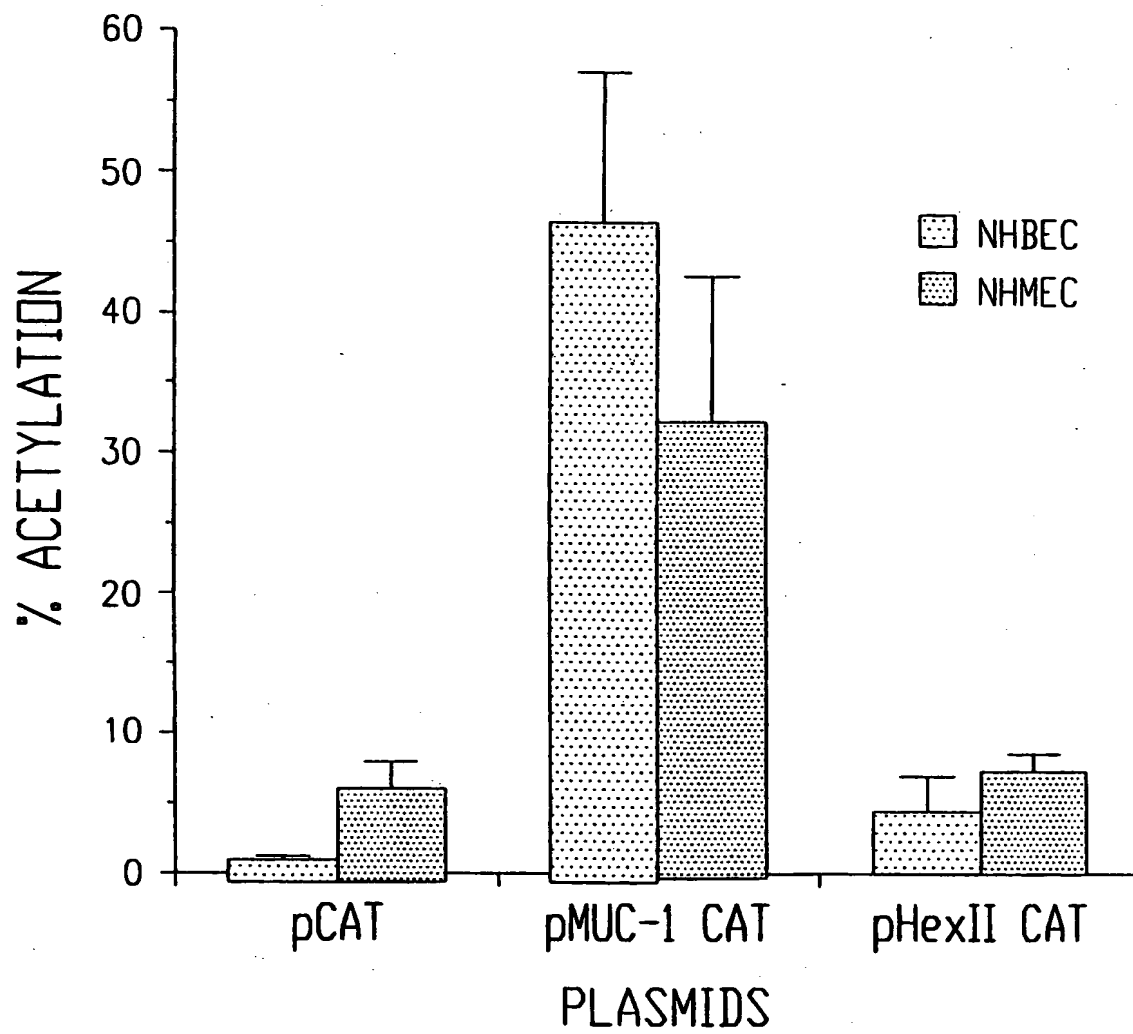


Fig. 4

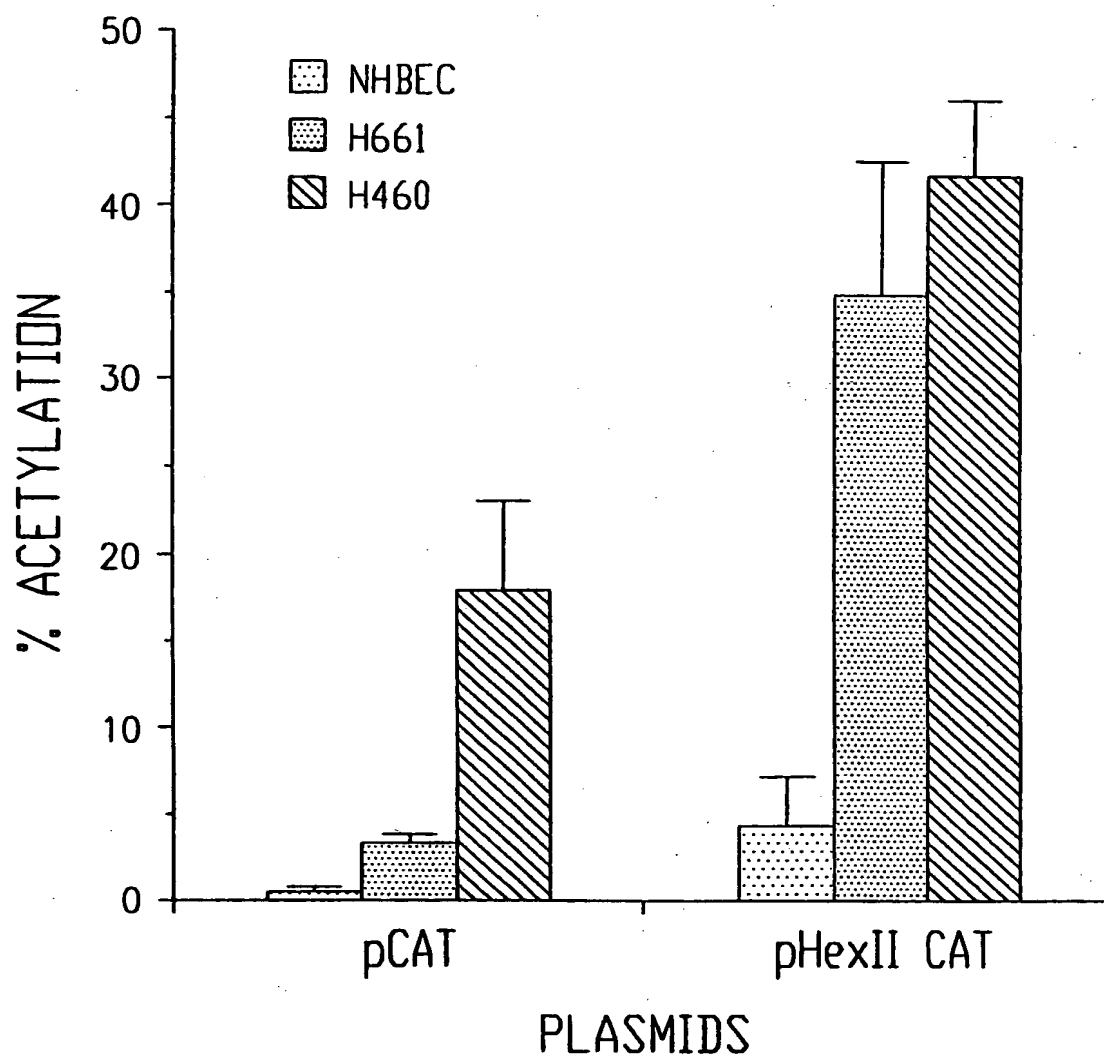


Fig. 5

09739223 121000

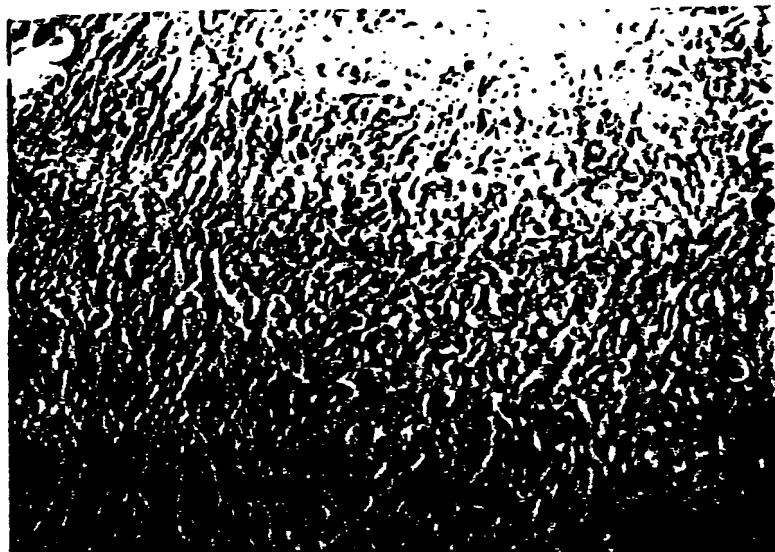


Fig. 6A



Fig. 6B

A high-contrast, black and white photograph showing a dense, textured surface, possibly a rock face or a heavily eroded wall. The image is characterized by a complex pattern of dark, irregular shapes and spots scattered across a lighter, grainy background, creating a highly textured and somewhat abstract appearance.

A high-contrast, black and white photograph showing a dense, textured surface, possibly a wall or a large rock face. The image is characterized by a multitude of small, dark, irregular shapes scattered across a lighter, grainy background, creating a complex, almost abstract pattern. The overall effect is one of intense texture and visual noise.

Fig. 6D

Fig. 6E

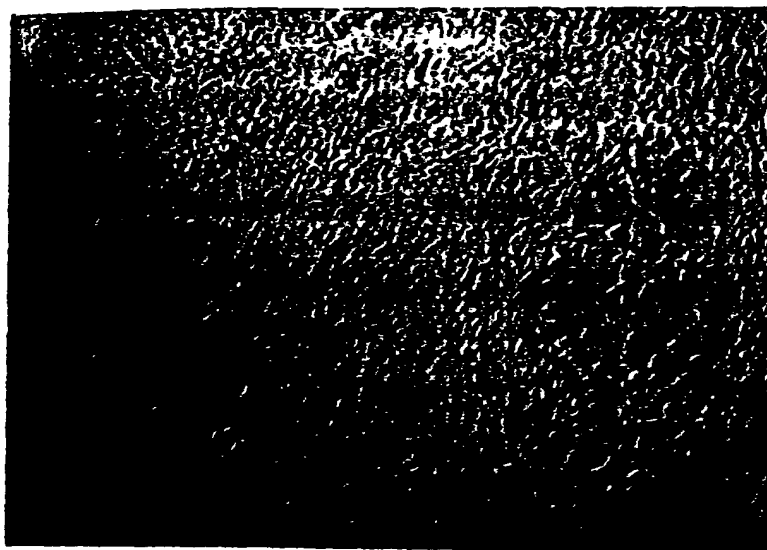
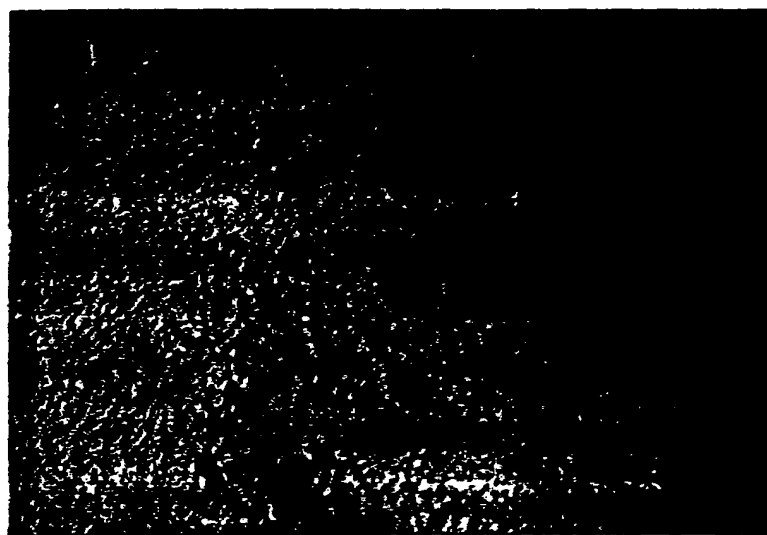


Fig. 6F



09739223.121800

A high-contrast, black and white photograph showing a dense, textured surface, possibly a crowd or a large group of people, with many small, bright highlights. The image is very dark, with the highlights creating a grainy, speckled appearance. The overall effect is one of a vast, unidentifiable mass of people or objects.

A high-contrast, black and white image showing a dense, textured surface. The texture is highly irregular and granular, with many small, bright, circular or oval features scattered throughout a dark background. The overall appearance is reminiscent of a microscopic view of a material or a close-up of a rough surface.

Fig. 6H

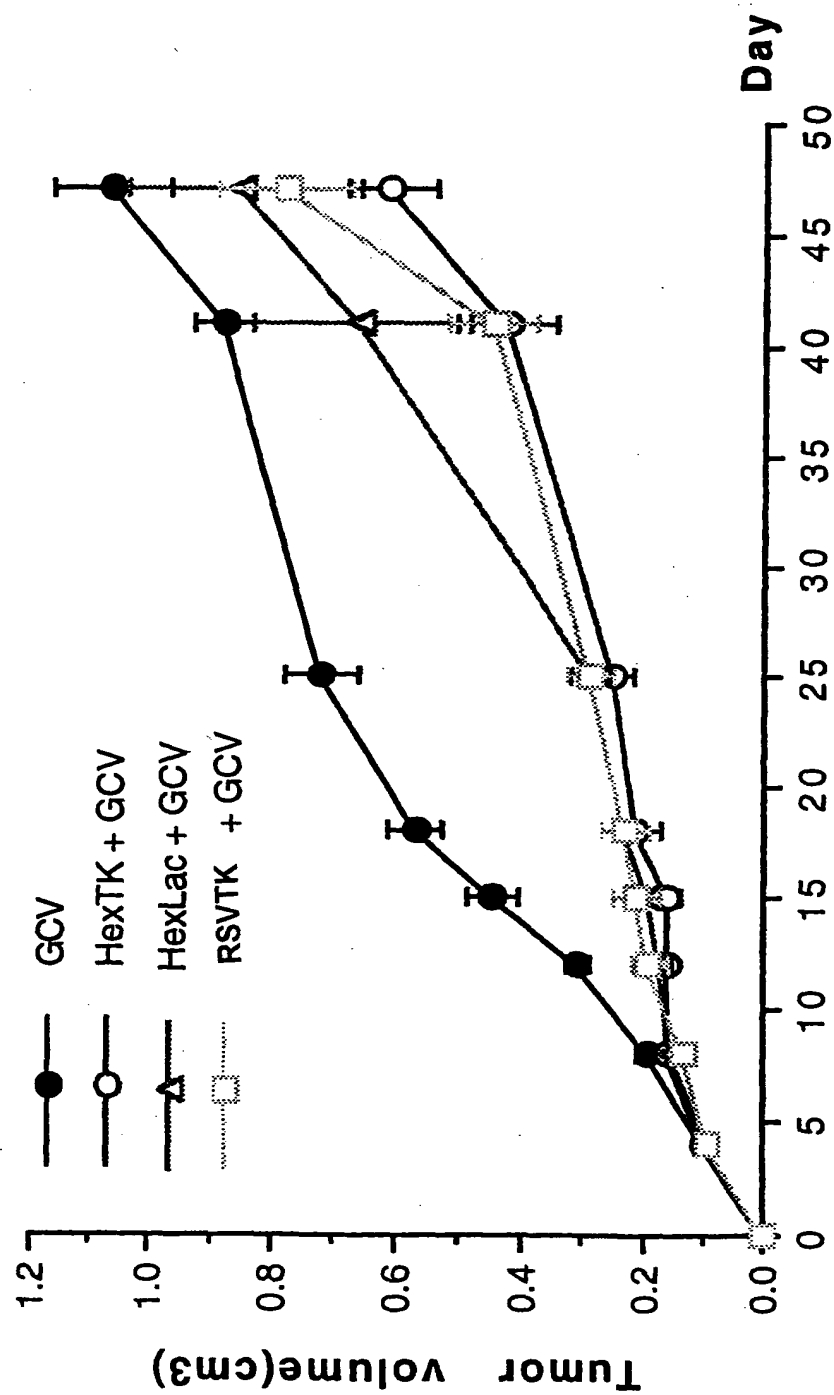


Fig. 7A

Tumor growth in DA3 mice treated with Adenovirus

| G1 GCVLP. | | | | | | | | | | G2 HxTK + GCV LP. | | | | | | | | | |
|---|------|-------|-------|-------|-------|-------|------|------|------|--|-------|-------|-------|-------|-------|------|------|--|--|
| d | 4 | 8 | 12 | 15 | 18 | 25 | 41 | 47 | d | 4 | 8 | 12 | 15 | 18 | 25 | 41 | 47 | | |
| date | 7/12 | 11/12 | 15/12 | 18/12 | 21/12 | 28/12 | 13/1 | 19/1 | date | 7/12 | 11/12 | 15/12 | 18/12 | 21/12 | 28/12 | 13/1 | 19/1 | | |
| #1 | 0.63 | 0.78 | 0.87 | 0.95 | 1.00 | 1.05 | 1.19 | 1.23 | #1 | 0.52 | 0.60 | 0.50 | 0.47 | 0.48 | 0.58 | 0.59 | 0.87 | | |
| #2 | 0.74 | 0.84 | 0.92 | 1.02 | 1.13 | 1.18 | 1.28 | 1.48 | | 0.65 | 0.72 | 0.78 | 0.60 | 0.55 | 0.65 | 0.76 | 0.98 | | |
| #3 | 0.52 | 0.75 | 0.80 | 1.06 | 1.14 | 1.22 | 1.20 | 1.18 | #2 | 0.60 | 0.63 | 0.56 | 0.54 | 0.58 | 0.66 | 0.93 | 1.00 | | |
| | 0.68 | 0.98 | 1.24 | 1.28 | 1.40 | 1.50 | 1.48 | 1.50 | | 0.62 | 0.72 | 0.78 | 0.74 | 0.78 | 0.90 | 1.13 | 1.30 | | |
| #3 | 0.48 | 0.53 | 0.66 | 0.78 | 0.75 | 0.88 | 1.01 | 1.18 | #3 | 0.60 | 0.63 | 0.55 | 0.47 | 0.48 | 0.56 | 0.68 | 0.85 | | |
| | 0.62 | 0.64 | 0.78 | 0.98 | 1.24 | 1.33 | 1.43 | 1.64 | | 0.70 | 0.74 | 0.68 | 0.92 | 0.68 | 0.78 | 0.82 | 1.02 | | |
| #4 | 0.44 | 0.56 | 0.82 | 0.98 | 1.00 | 8 | | | #4 | 0.58 | 0.67 | 0.67 | 0.58 | 0.60 | 0.67 | 0.73 | 0.80 | | |
| | 0.77 | 0.90 | 1.04 | 1.06 | 1.14 | 8 | | | | 0.67 | 0.74 | 0.70 | 0.72 | 0.73 | 0.82 | 0.93 | 1.07 | | |
| #5 | 0.48 | 0.65 | 0.82 | 0.90 | 1.03 | 1.08 | 1.12 | 1.13 | #5 | 0.50 | 0.64 | 0.53 | 0.47 | 0.50 | 0.60 | 0.58 | 0.82 | | |
| | 0.55 | 0.62 | 1.13 | 1.18 | 1.21 | 1.30 | 1.26 | 1.30 | | 0.68 | 0.72 | 0.94 | 0.72 | 1.02 | 0.97 | 1.08 | 1.15 | | |
| #6 | 0.58 | 0.60 | 0.72 | 0.80 | 0.78 | 1.08 | 1.22 | 1.37 | #6 | 0.58 | 0.72 | 0.77 | 0.74 | 0.75 | 0.74 | 0.78 | 0.94 | | |
| | 0.67 | 0.96 | 1.17 | 1.20 | 1.37 | 1.33 | 1.38 | 1.44 | | 0.64 | 0.75 | 0.92 | 0.92 | 0.95 | 1.02 | 1.23 | 1.28 | | |
| #7 | 0.53 | 0.62 | 0.66 | 0.73 | 0.88 | 0.85 | 1.04 | 1.19 | #7 | 0.58 | 0.64 | 0.67 | 0.64 | 0.73 | 0.84 | 0.94 | 0.98 | | |
| | 0.58 | 0.84 | 0.94 | 1.08 | 1.18 | 1.32 | 1.38 | 1.47 | | 0.63 | 1.04 | 0.97 | 0.66 | 0.96 | 1.08 | 1.21 | 1.20 | | |
| #8 | 0.58 | 0.73 | 0.90 | 0.95 | 1.03 | 8 | | | #8 | 0.45 | 0.62 | 0.68 | 0.82 | 0.90 | 0.86 | 1.18 | 1.28 | | |
| | 0.79 | 0.85 | 1.05 | 1.13 | 1.21 | 8 | | | | 0.60 | 0.78 | 1.03 | 1.10 | 1.28 | 1.37 | 1.50 | 1.57 | | |
| #9 | 0.57 | 0.65 | 0.68 | 0.78 | 0.92 | 1.04 | 1.08 | 1.07 | #9 | 0.56 | 0.65 | 0.54 | 0.58 | 0.66 | 0.67 | 0.67 | 1.03 | | |
| | 0.62 | 0.75 | 1.14 | 1.27 | 1.30 | 1.48 | 1.50 | 1.60 | | 0.73 | 0.82 | 0.93 | 0.95 | 0.97 | 0.94 | 1.19 | 1.27 | | |
| #10 | 0.52 | 0.60 | 0.73 | 0.88 | 0.95 | 0.97 | 1.02 | 1.00 | #10 | 0.52 | 0.64 | 0.58 | 0.58 | 0.57 | 0.65 | 0.93 | 0.96 | | |
| | 0.73 | 1.04 | 1.14 | 1.16 | 1.20 | 1.21 | 1.34 | 1.46 | | 0.65 | 0.97 | 1.08 | 0.94 | 0.92 | 1.20 | 1.18 | 1.28 | | |
| #11 | 0.50 | 0.57 | 0.60 | 0.64 | 0.77 | 1.08 | 1.13 | 1.25 | #11 | 0.52 | 0.64 | 0.66 | 0.73 | 0.88 | 0.65 | 1.01 | 1.15 | | |
| | 0.84 | 0.97 | 1.28 | 1.34 | 1.54 | 1.50 | 1.87 | 2.25 | | 0.58 | 0.83 | 0.98 | 1.06 | 1.06 | 1.10 | 1.48 | 1.46 | | |
| #12 | 0.56 | 0.82 | 0.92 | 1.04 | 1.08 | 1.06 | 1.10 | 1.12 | #12 | 0.48 | 0.58 | 0.52 | 0.50 | 0.54 | 0.68 | 0.61 | 0.90 | | |
| | 0.68 | 0.98 | 0.94 | 1.12 | 1.20 | 1.18 | 1.24 | 1.30 | | 0.58 | 0.67 | 0.95 | 0.92 | 0.97 | 1.03 | 1.20 | 1.12 | | |
| #1 | 0.15 | 0.26 | 0.35 | 0.46 | 0.57 | 0.65 | 0.91 | 1.12 | #1 | 0.09 | 0.13 | 0.10 | 0.07 | 0.06 | 0.11 | 0.13 | 0.37 | | |
| #2 | 0.09 | 0.28 | 0.40 | 0.72 | 0.91 | 1.12 | 1.07 | 1.04 | #2 | 0.11 | 0.14 | 0.12 | 0.11 | 0.13 | 0.20 | 0.49 | 0.65 | | |
| #3 | 0.07 | 0.08 | 0.17 | 0.30 | 0.35 | 0.51 | 0.73 | 1.14 | #3 | 0.13 | 0.15 | 0.10 | 0.07 | 0.08 | 0.12 | 0.19 | 0.37 | | |
| #4 | 0.07 | 0.14 | 0.35 | 0.48 | 0.57 | 8 | | | #4 | 0.11 | 0.17 | 0.16 | 0.12 | 0.13 | 0.18 | 0.25 | 0.43 | | |
| #5 | 0.06 | 0.17 | 0.38 | 0.48 | 0.64 | 0.76 | 0.79 | 0.83 | #5 | 0.09 | 0.15 | 0.12 | 0.08 | 0.13 | 0.17 | 0.18 | 0.39 | | |
| #6 | 0.11 | 0.17 | 0.30 | 0.38 | 0.42 | 0.78 | 1.03 | 1.35 | #6 | 0.11 | 0.19 | 0.24 | 0.25 | 0.27 | 0.28 | 0.36 | 0.57 | | |
| #7 | 0.08 | 0.16 | 0.20 | 0.29 | 0.46 | 0.48 | 0.75 | 1.04 | #7 | 0.11 | 0.21 | 0.22 | 0.18 | 0.26 | 0.38 | 0.53 | 0.58 | | |
| #8 | 0.12 | 0.23 | 0.43 | 0.51 | 0.64 | 8 | | | #8 | 0.06 | 0.15 | 0.24 | 0.37 | 0.52 | 0.51 | 1.04 | 1.29 | | |
| #9 | 0.10 | 0.18 | 0.26 | 0.38 | 0.55 | 0.79 | 0.87 | 0.92 | #9 | 0.11 | 0.17 | 0.14 | 0.16 | 0.21 | 0.21 | 0.45 | 0.67 | | |
| #10 | 0.10 | 0.18 | 0.30 | 0.45 | 0.64 | 0.57 | 0.70 | 0.73 | #10 | 0.09 | 0.20 | 0.18 | 0.16 | 0.15 | 0.25 | 0.51 | 0.59 | | |
| #11 | 0.11 | 0.16 | 0.23 | 0.27 | 0.46 | 0.87 | 1.19 | 1.76 | #11 | 0.08 | 0.17 | 0.21 | 0.28 | 0.41 | 0.40 | 0.75 | 0.97 | | |
| #12 | 0.11 | 0.30 | 0.40 | 0.61 | 0.70 | 0.65 | 0.76 | 0.82 | #12 | 0.07 | 0.11 | 0.13 | 0.12 | 0.14 | 0.24 | 0.22 | 0.45 | | |
| M | 0.10 | 0.19 | 0.31 | 0.45 | 0.57 | 0.72 | 0.88 | 1.07 | M | 0.10 | 0.16 | 0.16 | 0.16 | 0.21 | 0.25 | 0.43 | 0.61 | | |
| SD | 0.02 | 0.06 | 0.08 | 0.13 | 0.15 | 0.19 | 0.17 | 0.30 | SD | 0.02 | 0.03 | 0.05 | 0.09 | 0.14 | 0.12 | 0.27 | 0.27 | | |
| SEM | 0.01 | 0.02 | 0.02 | 0.04 | 0.04 | 0.06 | 0.05 | 0.10 | SEM | 0.01 | 0.01 | 0.01 | 0.02 | 0.04 | 0.03 | 0.08 | 0.07 | | |
| 5x10 ⁶ DA3 cells a.c. on 03/12/88(40). | | | | | | | | | | Ganciclovir(GCV) 100mg/kg Ip. 08-14/12/88(d8-d11). | | | | | | | | | |
| Adenovirus intratumoral injections on 08-10/12/88(C5- d17). | | | | | | | | | | | | | | | | | | | |

Fig. 7B

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Tumor growth in DA3 mice treated with Adenovirus

| G3 HexLac + GCV Ip. | | | | | | | | | | | G4 HexRSV + GCV Ip. | | | | | | | | | | |
|---------------------|------|-------|-------|-------|-------|-------|------|------|------|------|---------------------|-------|-------|-------|-------|------|------|----|--|--|--|
| d | 4 | 8 | 12 | 15 | 18 | 25 | 41 | 47 | date | d | 4 | 8 | 12 | 15 | 18 | 25 | 41 | 47 | | | |
| date | 7/12 | 11/12 | 15/12 | 18/12 | 21/12 | 28/12 | 13/1 | 19/1 | date | 7/12 | 11/12 | 15/12 | 18/12 | 21/12 | 28/12 | 13/1 | 19/1 | | | | |
| #1 | 0.53 | 0.64 | 0.60 | 0.57 | 0.65 | 0.68 | 0.80 | 0.92 | #1 | 0.50 | 0.54 | 0.53 | 0.55 | 0.53 | 0.62 | 0.74 | 0.97 | | | | |
| | 0.65 | 0.70 | 0.64 | 0.64 | 0.72 | 0.80 | 0.82 | 1.02 | | 0.68 | 0.90 | 1.06 | 0.98 | 1.04 | 1.03 | 1.16 | 1.13 | | | | |
| #2 | 0.60 | 0.70 | 0.65 | 0.60 | 0.70 | 0.70 | 0.77 | 0.85 | #2 | 0.48 | 0.65 | 0.60 | 0.57 | 0.53 | 0.70 | 1.06 | 1.28 | | | | |
| | 0.68 | 0.78 | 0.78 | 0.77 | 0.72 | 0.66 | 0.68 | 0.98 | | 0.73 | 0.78 | 1.18 | 1.18 | 1.10 | 1.28 | 1.80 | 1.88 | | | | |
| #3 | 0.58 | 0.66 | 0.57 | 0.63 | 0.66 | 0.73 | 1.04 | 1.16 | #3 | 0.67 | 0.74 | 0.80 | 0.90 | 0.93 | 0.88 | 0.79 | 1.00 | | | | |
| | 0.65 | 0.68 | 0.80 | 0.86 | 0.95 | 1.08 | 1.50 | 1.64 | | 0.78 | 0.80 | 1.06 | 1.12 | 1.16 | 1.18 | 1.38 | 1.45 | | | | |
| #4 | 0.48 | 0.48 | 0.57 | 0.60 | 0.64 | 0.77 | 0.90 | 0.93 | #4 | 0.57 | 0.58 | 0.55 | 0.56 | 0.55 | 0.66 | 0.76 | 0.83 | | | | |
| | 0.67 | 0.75 | 0.76 | 0.78 | 0.80 | 0.84 | 0.99 | 1.22 | | 0.76 | 0.80 | 0.82 | 0.60 | 0.62 | 0.74 | 1.00 | 1.02 | | | | |
| #5 | 0.56 | 0.72 | 0.67 | 0.67 | 0.73 | 0.80 | 1.23 | 1.28 | #5 | 0.48 | 0.50 | 0.64 | 0.70 | 0.78 | 0.78 | 0.88 | 1.30 | | | | |
| | 0.77 | 0.83 | 0.90 | 0.92 | 1.06 | 1.16 | 1.80 | 1.74 | | 0.73 | 0.80 | 0.92 | 0.86 | 0.88 | 1.00 | 1.35 | 1.37 | | | | |
| #6 | 0.47 | 0.62 | 0.58 | 0.60 | 0.70 | 0.84 | 1.40 | 1.47 | #6 | 0.45 | 0.45 | 0.45 | 0.43 | 0.40 | 0.48 | 0.54 | 0.60 | | | | |
| | 0.53 | 0.78 | 1.04 | 1.05 | 1.17 | 1.28 | 1.68 | 1.85 | | 0.53 | 0.58 | 0.55 | 0.48 | 0.48 | 0.62 | 0.60 | 0.78 | | | | |
| #7 | 0.52 | 0.60 | 0.72 | 0.75 | 0.88 | S | | S | #7 | 0.48 | 0.65 | 0.78 | 0.76 | 0.80 | 0.90 | 0.90 | 1.06 | | | | |
| | 0.72 | 0.78 | 0.80 | 0.94 | 1.18 | S | | S | | 0.80 | 0.77 | 0.88 | 0.87 | 0.85 | 0.98 | 1.02 | 1.13 | | | | |
| #8 | 0.45 | 0.60 | 0.65 | 0.70 | 0.74 | S | | S | #8 | 0.49 | 0.53 | 0.58 | 0.66 | 0.80 | 0.88 | 0.97 | 1.08 | | | | |
| | 0.50 | 0.85 | 1.05 | 1.06 | 1.17 | S | | S | | 0.67 | 0.85 | 1.03 | 1.10 | 1.12 | 1.14 | 1.25 | 1.47 | | | | |
| #9 | 0.50 | D | | | | | | D | #9 | 0.54 | 0.57 | 0.55 | 0.57 | 0.60 | 0.67 | 0.76 | 1.00 | | | | |
| | 0.63 | D | | | | | | D | | 0.60 | 0.68 | 0.96 | 1.00 | 1.04 | 1.12 | 1.50 | 1.55 | | | | |
| #10 | 0.48 | 0.65 | 0.73 | 0.68 | 0.70 | 0.74 | 0.84 | 0.92 | #10 | 0.47 | 0.50 | 0.52 | 0.50 | 0.50 | 0.57 | 0.71 | 1.12 | | | | |
| | 0.66 | 0.78 | 0.80 | 1.02 | 1.03 | 1.07 | 1.20 | 1.23 | | 0.65 | 1.05 | 1.18 | 0.94 | 0.72 | 0.74 | 1.10 | 1.28 | | | | |
| #11 | 0.54 | 0.62 | 0.72 | 0.68 | 0.70 | 0.73 | 0.85 | 1.03 | #11 | 0.52 | 0.57 | 0.56 | 0.54 | 0.57 | 0.68 | 0.73 | 0.86 | | | | |
| | 0.58 | 0.70 | 0.80 | 1.06 | 1.12 | 1.28 | 1.20 | 1.42 | | 0.60 | 0.68 | 0.93 | 0.88 | 0.96 | 1.02 | 1.40 | 1.32 | | | | |
| #12 | 0.55 | 0.56 | 0.58 | 0.57 | 0.60 | 0.67 | 0.72 | 0.90 | #12 | 0.48 | 0.63 | 0.82 | 0.85 | 0.87 | 0.90 | 0.87 | 1.17 | | | | |
| | 0.58 | 0.73 | 0.78 | 0.82 | 0.87 | 1.06 | 1.25 | 1.25 | | 0.77 | 0.80 | 1.07 | 1.17 | 1.35 | 1.40 | 1.74 | 1.80 | | | | |
| #1 | 0.08 | 0.14 | 0.12 | 0.10 | 0.15 | 0.18 | 0.26 | 0.43 | #1 | 0.09 | 0.13 | 0.15 | 0.15 | 0.15 | 0.20 | 0.32 | 0.53 | | | | |
| #2 | 0.12 | 0.18 | 0.16 | 0.14 | 0.18 | 0.21 | 0.26 | 0.35 | #2 | 0.08 | 0.16 | 0.21 | 0.19 | 0.15 | 0.31 | 1.01 | 1.54 | | | | |
| #3 | 0.11 | 0.15 | 0.13 | 0.17 | 0.21 | 0.28 | 0.81 | 1.10 | #3 | 0.18 | 0.22 | 0.34 | 0.45 | 0.50 | 0.46 | 0.43 | 0.73 | | | | |
| #4 | 0.08 | 0.09 | 0.12 | 0.14 | 0.16 | 0.25 | 0.40 | 0.53 | #4 | 0.12 | 0.13 | 0.12 | 0.09 | 0.09 | 0.18 | 0.29 | 0.35 | | | | |
| #5 | 0.12 | 0.22 | 0.20 | 0.21 | 0.28 | 0.37 | 1.36 | 1.43 | #5 | 0.08 | 0.10 | 0.19 | 0.21 | 0.27 | 0.30 | 0.52 | 1.16 | | | | |
| #6 | 0.08 | 0.15 | 0.17 | 0.19 | 0.29 | 0.45 | 1.65 | 2.00 | #6 | 0.05 | 0.08 | 0.08 | 0.04 | 0.04 | 0.07 | 0.08 | 0.14 | | | | |
| #7 | 0.10 | 0.14 | 0.21 | 0.26 | 0.27 | S | | | #7 | 0.09 | 0.16 | 0.27 | 0.25 | 0.27 | 0.40 | 0.41 | 0.63 | | | | |
| #8 | 0.05 | 0.15 | 0.22 | 0.26 | 0.32 | S | | | #8 | 0.08 | 0.12 | 0.17 | 0.24 | 0.36 | 0.44 | 0.59 | 0.86 | | | | |
| #9 | 0.08 | D | | | | | | | #9 | 0.09 | 0.11 | 0.15 | 0.16 | 0.19 | 0.25 | 0.43 | 0.78 | | | | |
| #10 | 0.08 | 0.18 | 0.21 | 0.24 | 0.25 | 0.29 | 0.42 | 0.52 | #10 | 0.07 | 0.13 | 0.16 | 0.12 | 0.09 | 0.12 | 0.28 | 0.80 | | | | |
| #11 | 0.08 | 0.13 | 0.21 | 0.25 | 0.27 | 0.34 | 0.43 | 0.75 | #11 | 0.08 | 0.11 | 0.15 | 0.13 | 0.16 | 0.24 | 0.37 | 0.61 | | | | |
| #12 | 0.08 | 0.11 | 0.13 | 0.13 | 0.16 | 0.24 | 0.32 | 0.51 | #12 | 0.08 | 0.16 | 0.38 | 0.42 | 0.51 | 0.57 | 0.66 | 1.23 | | | | |
| M | 0.09 | 0.15 | 0.17 | 0.19 | 0.23 | 0.29 | 0.66 | 0.85 | M | 0.09 | 0.13 | 0.19 | 0.21 | 0.23 | 0.29 | 0.45 | 0.78 | | | | |
| SD | 0.02 | 0.03 | 0.04 | 0.06 | 0.06 | 0.08 | 0.51 | 0.58 | SD | 0.03 | 0.04 | 0.09 | 0.12 | 0.16 | 0.15 | 0.23 | 0.39 | | | | |
| SEM | 0.01 | 0.01 | 0.01 | 0.02 | 0.02 | 0.03 | 0.17 | 0.19 | SEM | 0.01 | 0.01 | 0.03 | 0.04 | 0.04 | 0.04 | 0.07 | 0.11 | | | | |

5x10⁶ DA3 cells s.c. on 03/12/88(d0). Ganciclovir(GCV) 100mg/kg Ip. 09-14/12/88(d6-d11).

Adenovirus intratumoral injections on 08, 10/12/88(d5, d17).

Fig. 7C

000727 22262260

Strategy for generating the HK II promoter reporter gene construct
pHexII4557 CAT, and pUC/HexII/LacZ and pAdBN/HexLacZ

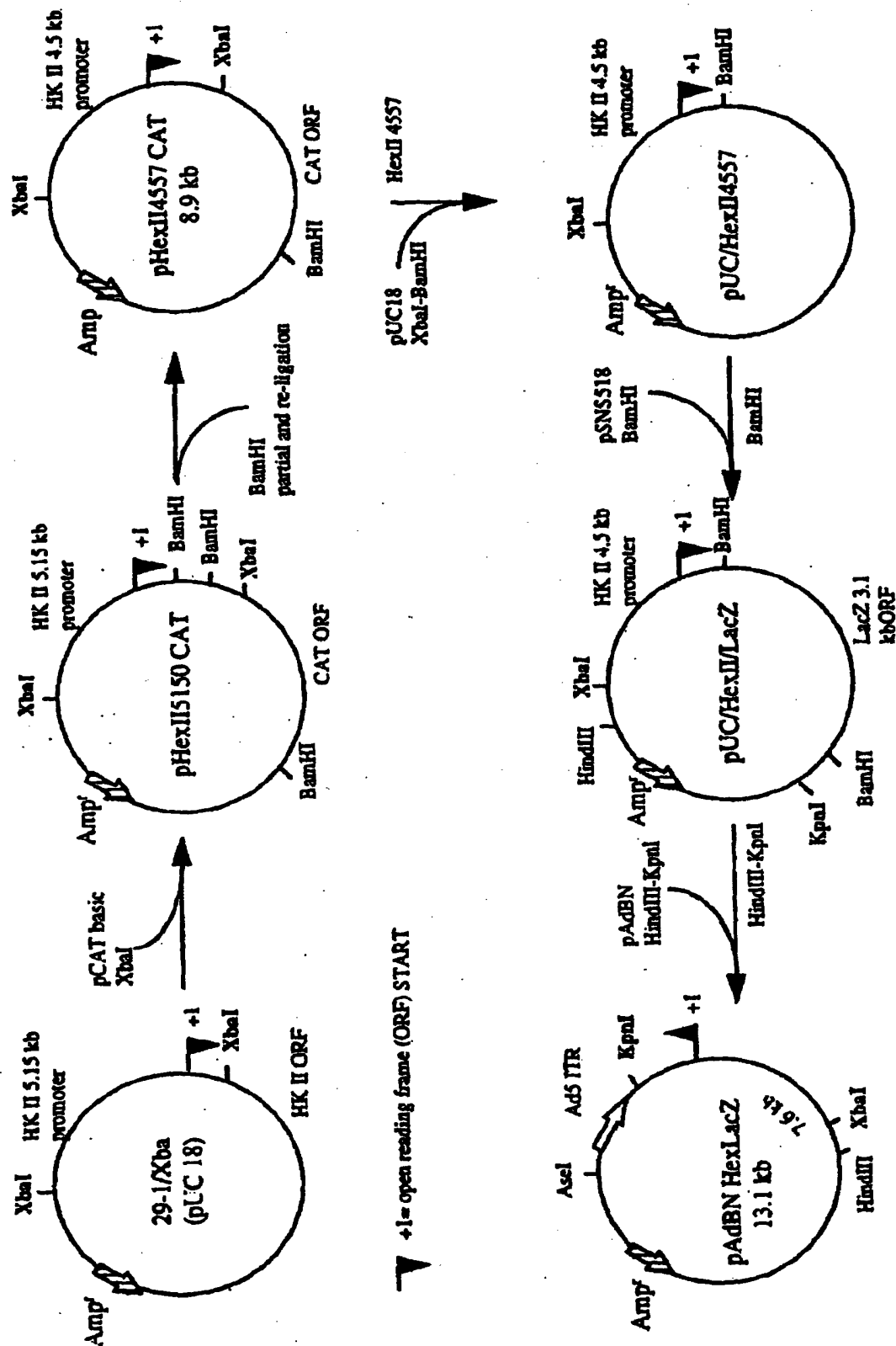


Fig. 8

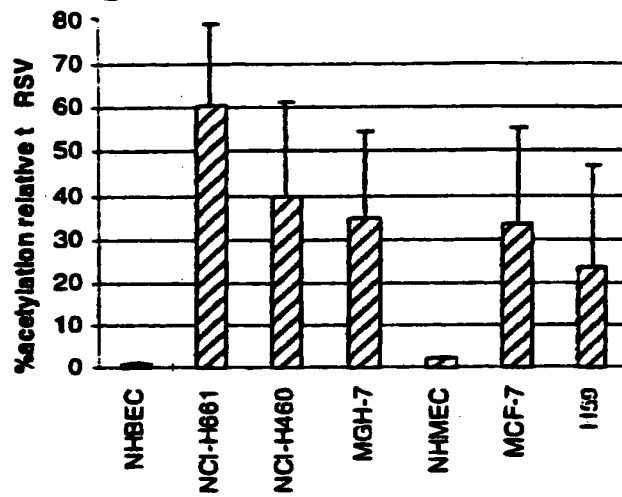


Fig. 9A

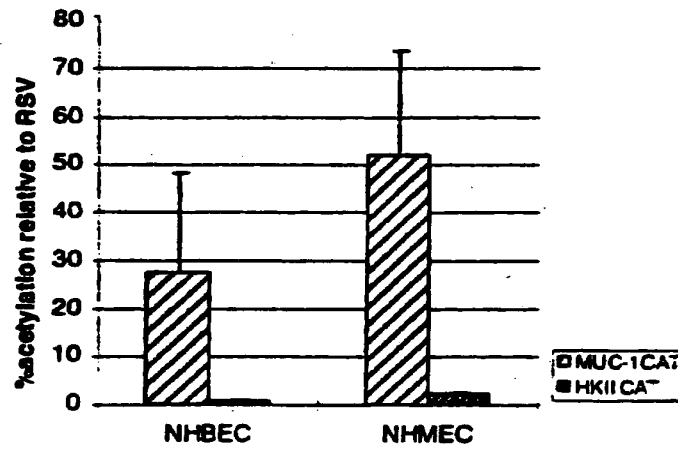


Fig. 9B

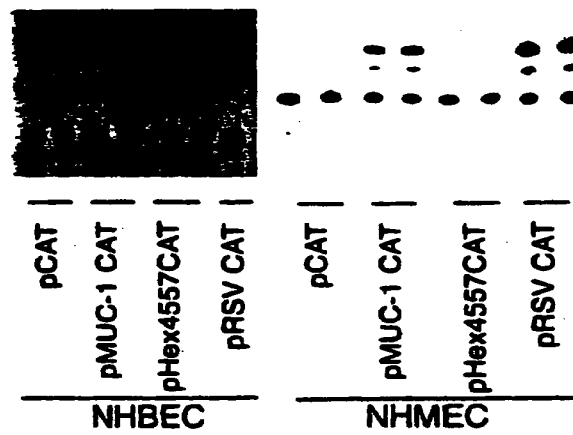


Fig. 9C

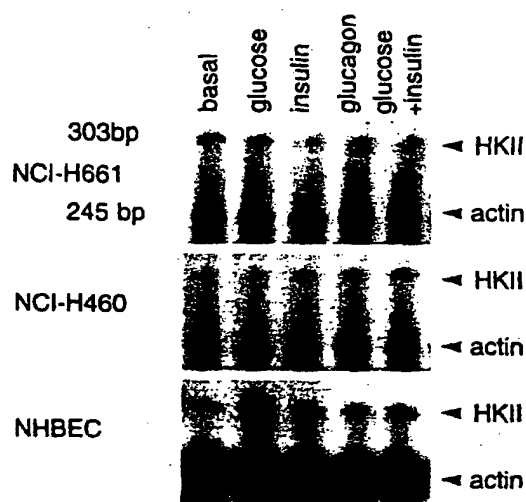


Fig. 10A

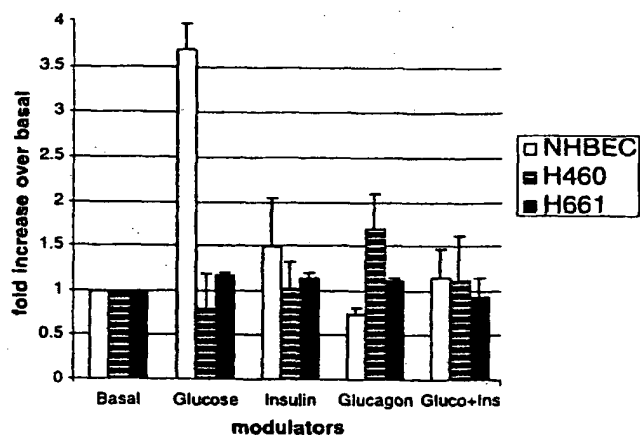


Fig. 10B

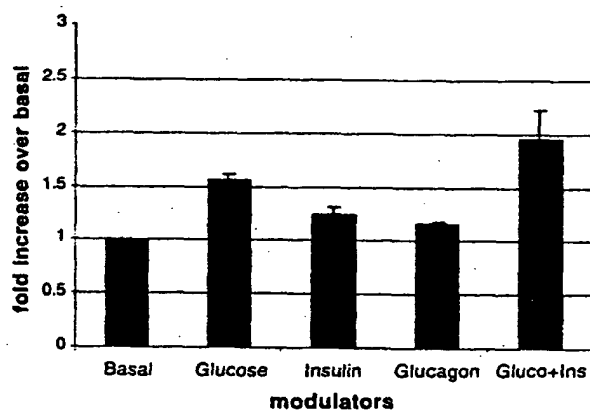


Fig. 10C



Fig. 11A

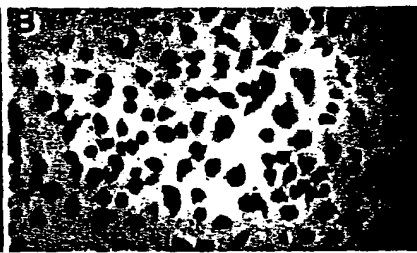


Fig. 11B

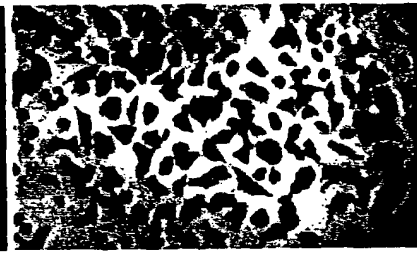


Fig. 11C

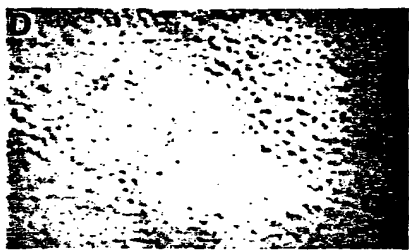


Fig. 11D

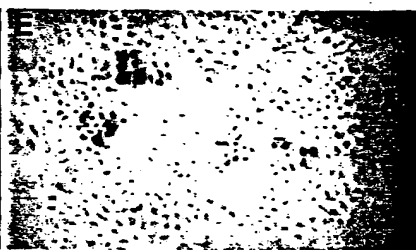


Fig. 11E

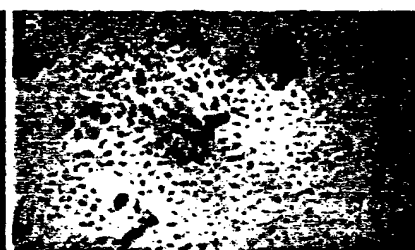


Fig. 11F

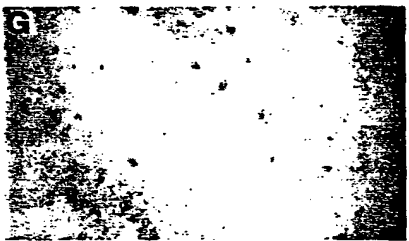


Fig. 11G

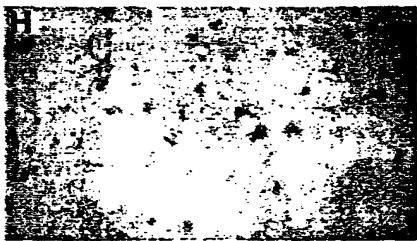


Fig. 11H

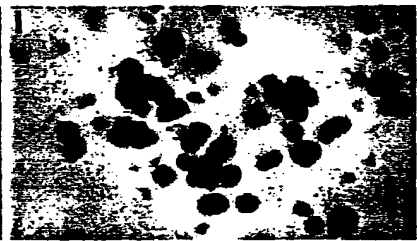


Fig. 11I

00700223 121800

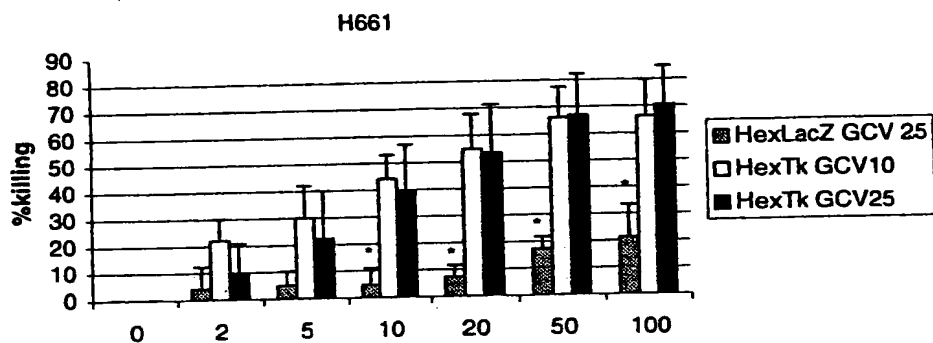


Fig. 12A

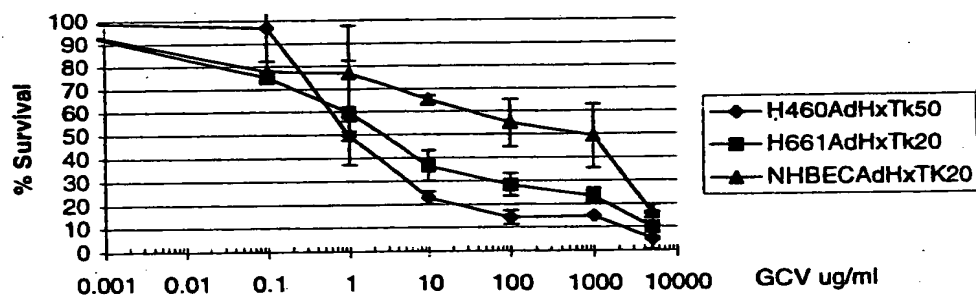


Fig. 12B

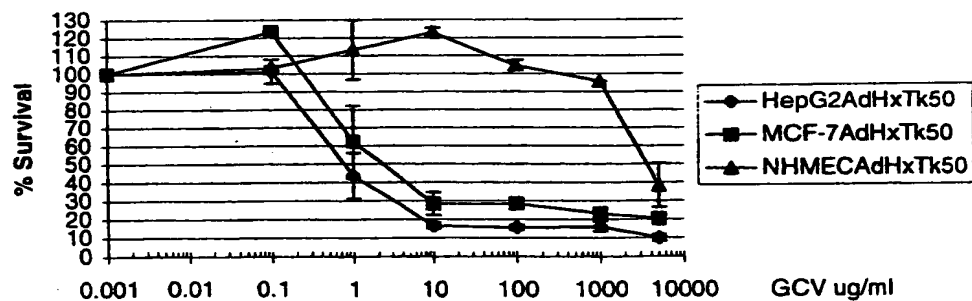


Fig. 12C